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REVIEW

Prone positioning in ARDS

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Abstract

Over the past five decades, prone positioning has evolved from single case reports to an evidence-based intervention. Initially used as a rescue therapy, it is now recognized as an integral component of lung-protective mechanical ventilation strategies, applied early in intubated patients with acute respiratory distress syndrome (ARDS) with a PaO_2/F_IO_2 ratio < 150 mmHg. The COVID-19 pandemic further expanded its use to non-intubated patients, the so-called awake prone position (APP), with promising results. APP requires confirmation in non-COVID patients and in a more routine ICU practice. Improved oxygenation is a consistent and well-recognized effect of prone positioning in both intubated and non-intubated patients with ARDS. Beyond its effects on gas exchange, prone positioning mitigates ventilator-induced lung injury by reducing lung stress and strain and may also confer favorable hemodynamic effects. This article reviews the physiologic rationale for prone positioning, evidence from randomized controlled trials, current guideline recommendations, practical aspects of implementation, and ongoing questions in both intubated and non-intubated patients.

Keywords: Acute hypoxemic respiratory failure, Hypoxemia, Ventilator-induced lung injury, Acute respiratory distress syndrome, Prone positioning

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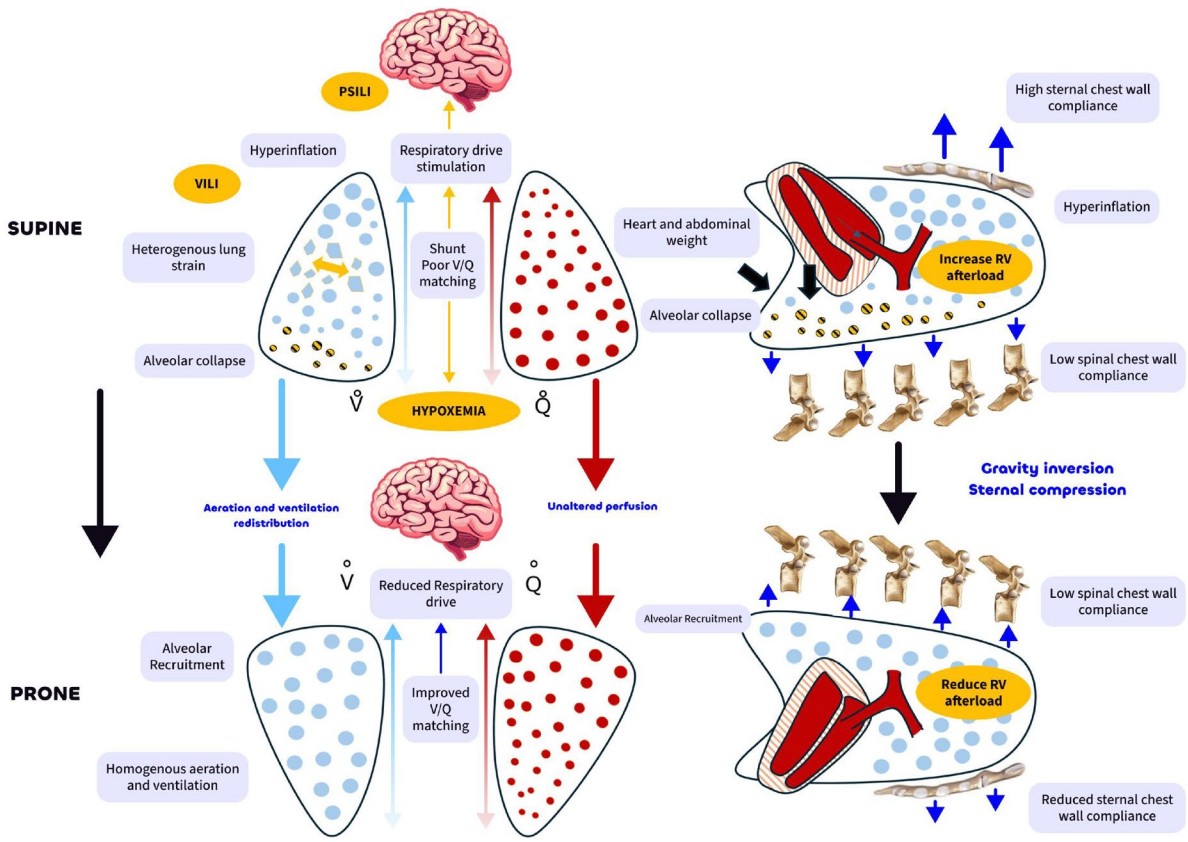
Visual abstract:

PRONE POSITIONING IN ARDS



Findings

- **From rescue therapy to standard of care:** how prone positioning became a cornerstone of ARDS management, supported by decades of physiological and clinical evidence.
- **Beyond oxygenation:** learn why the benefit of prone positioning extends far beyond improved gas exchange, reducing lung injury and improving cardiopulmonary physiology.
- **Intubated and awake patients:** practical implementation and remaining controversies for both conventional and awake prone positioning.
- **What have we learned from COVID-19?** How the pandemic transformed prone positioning practice and what lessons should shape future respiratory pandemics.

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Take home message

Prone positioning has evolved from a rescue maneuver to a cornerstone intervention in the management of ARDS. High-quality evidence has demonstrated a mortality benefit in selected intubated patients with moderate-to-severe ARDS. Promising results have also been observed in awake, non-intubated patients, particularly during the COVID-19 pandemic. Despite strong guideline recommendations, implementation of prone positioning remains inconsistent worldwide.

Introduction

First described in 1976 for mechanically ventilated patients with acute respiratory distress syndrome (ARDS) [1], prone positioning (PP) has evolved from a rescue therapy into a cornerstone of evidence-based management. While initially used to improve oxygenation in refractory hypoxemia, its clinical role remained controversial for decades due to inconsistent findings across early trials. This paradigm shifted following the landmark PROSEVA trial in 2013, which demonstrated a significant mortality benefit when PP was used early and for prolonged durations ($\geq$16 h) in patients with moderate-to-severe ARDS [2].

The clinical application of PP expanded further during the coronavirus disease 2019 (COVID-19) pandemic, with its widespread use in non-intubated patients, commonly referred to as "awake prone positioning (APP)" [3]. Currently, PP is considered an integral component of lung-protective strategies and is recommended by both the 2017 ATS/ESICM/SCCM clinical practice guidelines for severe ARDS [4] and the 2023 ESICM guidelines [5] for patients with moderate-to-severe ARDS. This article reviews the physiologic rationale for PP, evidence from randomized controlled trials (RCTs), current guideline recommendations, practical aspects of clinical implementation, and ongoing questions in both intubated and non-intubated patients.

Pathophysiology of prone position in patients with ARDS

Intubated patients

Improvement in oxygenation with PP has long been the most consistent and clinically apparent effect, both in frequency and magnitude. This effect essentially stems from a better matching between lung ventilation and perfusion [6], particularly in dorsal lung regions which are gravity-dependent in supine position (Fig. 1). In PP, redistribution of gravitational forces and relief of cardiac and mediastinal compression reduce superimposed pressure on dependent lungs, promoting alveolar recruitment and more homogeneous lung aeration [7–9]. Beyond gas exchange, PP contributes to lung protection by reducing ventral over-distension [10–12] and regional stress and strain. PP may also exert beneficial hemodynamic effects, including a reduced right ventricle afterload [13] and increased venous return and, hence cardiac output in preload-dependent patients [14].

Optimal ventilator management during PP remains an area of ongoing investigation. In clinical practice, fraction of inspired oxygen (F_IO_2) is often reduced in response to oxygenation improvement. Adjustment of positive end-expiratory pressure (PEEP) may be guided by trans-pulmonary pressure, as higher chest wall elastance in PP can cause airway pressure to overestimate true lung stress, or by electrical impedance tomography (EIT), which can assess regional ventilation [15] and support efforts to maintain lung recruitment after resupination. However, these physiological considerations are not yet supported by strong clinical evidence.

Non-intubated patients

Although the overall physiologic effects of APP, particularly improved oxygenation and ventilation–perfusion matching, are broadly similar to those observed in intubated ARDS (Table S1), regional ventilation patterns may differ, because spontaneous breathing is preserved. In a prospective cohort study, non-intubated patients demonstrated more homogeneous ventilation during APP without significant regional redistribution, contrasting with the dorsal redistribution typically observed in intubated patients [16]. In patients receiving conventional oxygen therapy or high-flow nasal cannula (HFNC), APP has been associated with improved ventilation–perfusion matching and modest improvements in lung aeration [17, 18]. Hemodynamic changes, including increased cardiac index, have also been reported, suggesting that improvements in pulmonary perfusion may contribute to the oxygenation response [19]. Interestingly, these physiologic effects appear more pronounced when APP is applied with HFNC or conventional oxygen therapy [10], whereas studies combining APP with continuous positive airway pressure (CPAP) or noninvasive ventilation (NIV) generally report minimal additional changes in ventilation distribution or lung aeration (Table S1). One possible explanation is that CPAP and NIV already provide relatively high levels of positive airway pressure that promote alveolar recruitment, thereby limiting the additional recruitment effect of APP.

The impact of APP on respiratory effort and its potential to prevent patient self-inflicted lung injury remain uncertain. Across studies involving different respiratory support modalities, work of breathing has generally been reported to decrease or remain unchanged, whereas esophageal pressure swings, a marker of inspiratory effort, have been reported to increase or remain unchanged

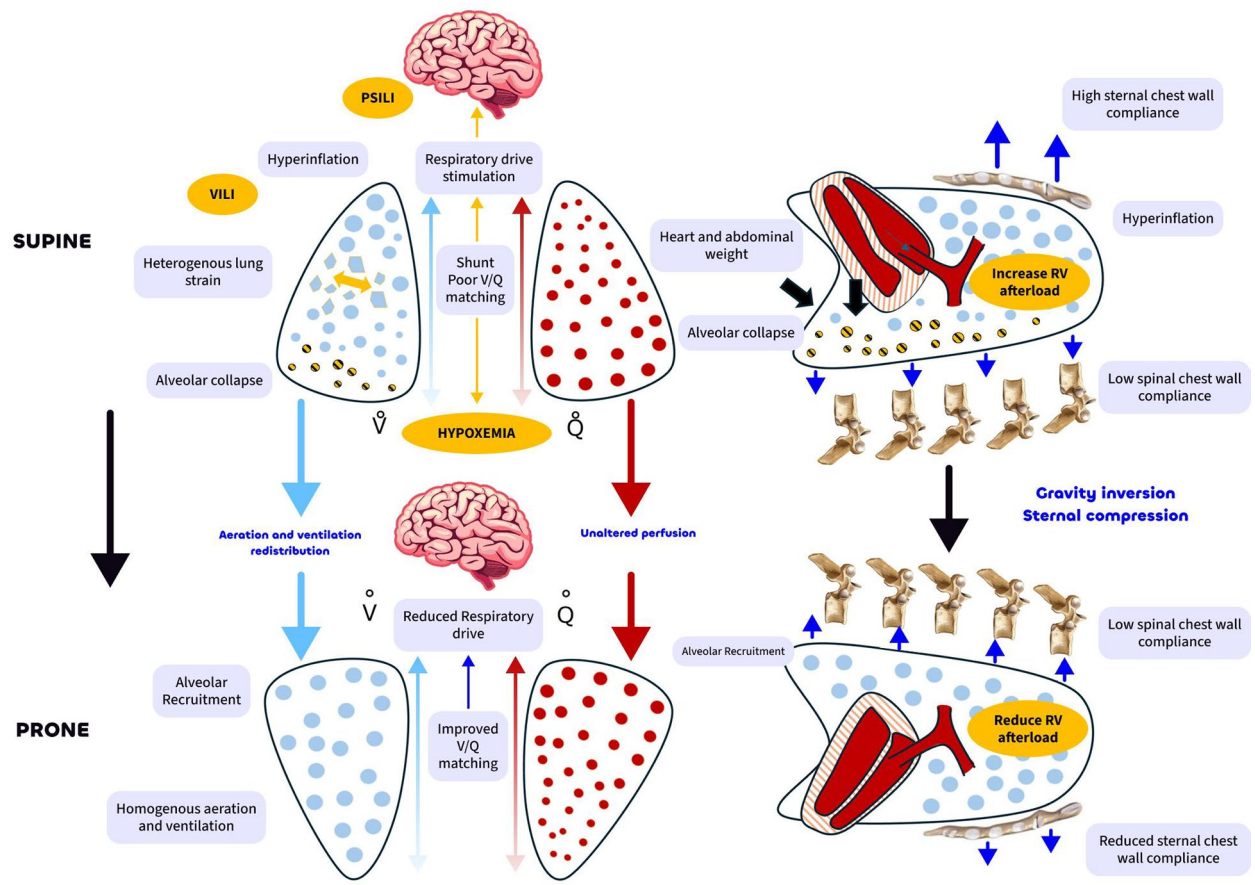

Fig. 1 Physiology of prone positioning. Mechanisms by which prone positioning can improve oxygenation, contribute to preventing lung injury and unloading the right ventricle in patients with acute respiratory distress syndrome. *VILI* ventilator-induced lung injury, *PSILI* patient self-inflicted lung injury, $\dot{V}$ lung ventilation, $\dot{Q}$ lung perfusion

(Table S1). This discrepancy may reflect differences between global work of breathing and breath-by-breath inspiratory effort. Improvements in oxygenation and ventilatory efficiency during APP may reduce respiratory rate and minute ventilation requirements, thereby lowering overall work of breathing despite unchanged or increased inspiratory effort per breath. These heterogeneous findings highlight the complex interaction between APP, respiratory mechanics, and patient respiratory drive in spontaneously breathing patients.

Historical perspective of clinical studies on prone position

In intubated patients

It took nearly 25 years from early reports of PP to the first RCT published in 2001 [20] (Table 1), just 1 year after the landmark ARMA trial highlighting the use of lower tidal volume [21] (Fig. 2). Early clinical interest in PP was largely driven by its consistent effect on improving oxygenation. However, the first two RCTs failed to demonstrate a survival benefit [20, 22]. Notably, both studies used large tidal volume (8–10 ml/kg measured body weight) and short PP sessions (7–8 h), without standardized ventilatory strategies. Two further trials introduced prolonged PP session (up to 18 h), used lung-protective ventilation, enrolled more hypoxemic patients but again failed to demonstrate a significant survival benefit perhaps by a lack of power [23, 24]. However, the individual patient data meta-analysis of these 4 trials demonstrated improved survival among patients with the most severe hypoxemia ($PaO_2/F_IO_2 < 100$ mmHg at the time of randomization) [25]. Finally, Guérin et al. [2] designed a RCT, whose specific features included intubation for less than 36 h, $PaO_2/F_IO_2 < 150$ mmHg with PEEP $\geq 5 cmH_2O$ and $F_IO_2 \geq 0.60$ and 6 ml/kg predicted body weight tidal volume confirmed after a stabilization period, lung-protective ventilation, long PP sessions (≥ 16 h), predetermined criteria to stop PP ($PaO_2/F_IO_2 \geq 150$ mmHg with PEEP $\leq 10 cmH_2O$ and $F_IO_2 \leq 0.60$ 4 h after resupination), use of neuromuscular

Table 1 Key randomized controlled trials of prone positioning in intubated and in non-intubated patients

Author	Years	Population and sample size[a]	Prone duration (h/day)	Tidal volume setting	Primary outcome	Key findings
Intubated patients						
Gattinoni et al. [20]	2001	304 ARDS	~ 6–7	10 ml/kg actual body weight	10-day mortality	Improved oxygenation but no mortality benefit at 10 days (21.1% vs 25.0%) and at ICU discharge (50.7% vs 48.0%)
Guérin et al. [22]	2004	791 patients (167 ALI, 246 ARDS)	~ 8	8 ml/kg actual body weight	28-day mortality	Improved oxygenation and reduced VAP incidence, but no significant difference in mortality (32.4% vs 31.5%, $p = 0.77$)
Mancebo et al. [23]	2006	136 severe ARDS	~ 20	8 ml/kg actual body weight	ICU mortality	Trend toward mortality reduction but not statistically significant (43% vs 58%, $p = 0.12$)
Taccone et al. [24]	2009	342 moderate–severe ARDS	~ 20	8 ml/kg PBW	28-day mortality	No significant mortality reduction overall at 28 days (31.0% vs 32.8%, $p = 0.72$)
Guérin et al. (PROSEVA) [2]	2013	466 severe ARDS ($PaO_2/FiO_2 < 150$ mmHg)	≥ 16	6 ml/kg PBW	28-day mortality	Significant mortality reduction at 28 days (16.0% vs 32.8%, $p < 0.001$) and at 90 days (23.6% vs 41.0%, $p < 0.001$)
Schmidt et al. [83]	2023	170 severe ARDS supported by VV-ECMO	16	3 ml/kg PBW	60-day successful ECMO weaning	No difference in 60-day successful ECMO weaning (44% vs 44%) and 90-day mortality (51% vs 48%, $p = 0.62$)
Non-intubated patients						
Ehrmann et al. [34]	2021	1121 COVID-19 patients requiring HFNC	5.0 (1.6–8.8)	HFNC	Intubation or death within 28 days	Reduced intubation rates (33% vs 44%) without signal of harm
Rampon et al. [35]	2022	293 COVID-19 on < 6 L/min oxygen	Not reported	COT / room air / HFNC	Respiratory deterioration (an increase in supplemental oxygen requirement) or ICU transfer	No significant reduction in respiratory deterioration or ICU transfer (22.1% vs 24.7%)
Alhazzani et al. [36]	2022	400 COVID-19 requiring oxygen therapy $FiO_2 \geq 0.4$ or NIV	4.8 (1.8–8.0)	COT / HFNC/ NIV	Intubation within 30 days	No significant difference in 30-day intubation rate (34.1% vs 40.5%, $p = 0.20$) and 60-day mortality (22% vs 24%, $p = 0.72$)
Fralick et al. [37]	2022	248 COVID-19 requiring oxygen therapy $FiO_2 \leq 0.5$	2 (0.5–4.2)	COT/HFNC	Composite of in-hospital death, mechanical ventilation, or worsening respiratory failure	No significant difference in the composite outcome (14% vs 14%)
Nay et al. [38]	2023	268 COVID-19 needs oxygen therapy in medical wards	2.3 (1.5–2.9)	COT/HFNC	Composite of need for NIV or intubation or died within 28 days	No significant difference in the composite outcome (14.1% vs 12.9%)
Liu et al. [39]	2024	409 COVID-19 patients	12 (12–14)	COT/HFNC/NIV	Intubation within 28 days	Reduced intubation rates (17% vs 27%)

Table 1 (continued)

Author	Years	Population and sample size[a]	Prone duration (h/day)	Tidal volume setting	Primary outcome	Key findings
Harrois et al. [40]	2025	445 COVID-19 patients	6 (2–8)	COT/HFNC/NIV	Intubation or death at 28 days	In Bayesian analysis high posterior probability of reduction in the primary outcome: 93.8% (mean odds ratio 0.74, 95% credible interval, 0.48–1.09)

ARDS actue respiratory distress syndrome, *ALI* acute lung injury, *HFNC* high-flow nasal cannula, *COT* conventional oxygen therapy, *NIV* noninvasive ventilation, *PBW* predicted body weight, *VV-ECMO* veno-venous extracorporeal membrane oxygenation, *COVID-19* coronavirus disease 2019, *VAP* ventilator-associated pneumonia, F_iO_2 fraction of inspired oxygen [a]Sample size for intention-to-treat analysis

blocking agents in the majority of patients in both groups, and avoidance of cross-over to PP in the supine group. As soon as the improvement criteria were obtained neuromuscular blocking agent (NMBA), if present, then sedation were stopped. This trial demonstrated a significant reduction in mortality [2]. This historical trajectory illustrates how the trials and trialists reciprocally enriched each other, the tight interaction between the clinical and experimental realms and the ultimate search of a population target. The ESICM guidelines discussed below made a strong recommendation to use PP according to the data of the PROSEVA trial. Indeed, the elegant leave-out meta-analysis made by Poole et al. clearly showed that the PROSEVA trial was an outlier, which completely matches the hypothesis, the reasoning and the design subtending this study [26].

In non-intubated patients

In contrast, the evolution of APP occurred over a much shorter time frame, largely driven by the COVID-19 pandemic. Prior to the pandemic, evidence was limited to small retrospective case studies showing that APP was feasible and improved oxygenation, without demonstrating effects on clinically meaningful outcomes [27]. The study by Ding et al., conducted between 2018 and 2019, represented an important step by prospectively evaluating APP in patients with moderate-to-severe ARDS receiving HFNC or NIV, suggesting a potential reduction in intubation rates [28]. The COVID-19 pandemic then acted as a catalyst for rapid clinical adoption and evidence generation. Numerous observational studies confirmed the feasibility of APP and consistently demonstrated improvements in oxygenation, with signals suggesting reduced intubation and mortality [3, 29–31]. This was accompanied by widespread dissemination of clinical experiences, further accelerating its use. To address the urgent need for high-quality evidence, several RCTs were initiated in the early pandemic. An international collaborative group implemented an innovative "meta-trial" design, harmonizing protocols across independent studies to prospectively pool data and perform interim analyses until pre-agreed efficacy or futility boundaries were met [32–34]. This effort included 1,121 COVID-19 patients receiving HFNC across six countries and was stopped early for benefit, demonstrating a reduction in treatment failure (intubation or death), thereby providing the first high-level evidence supporting APP. However, despite these landmark findings, the clinical efficacy of APP remains a subject of debate due to significant heterogeneity in results across subsequent RCTs [35–40] (Table 1). This variability underscores a critical dose–response effect, where the success of APP is

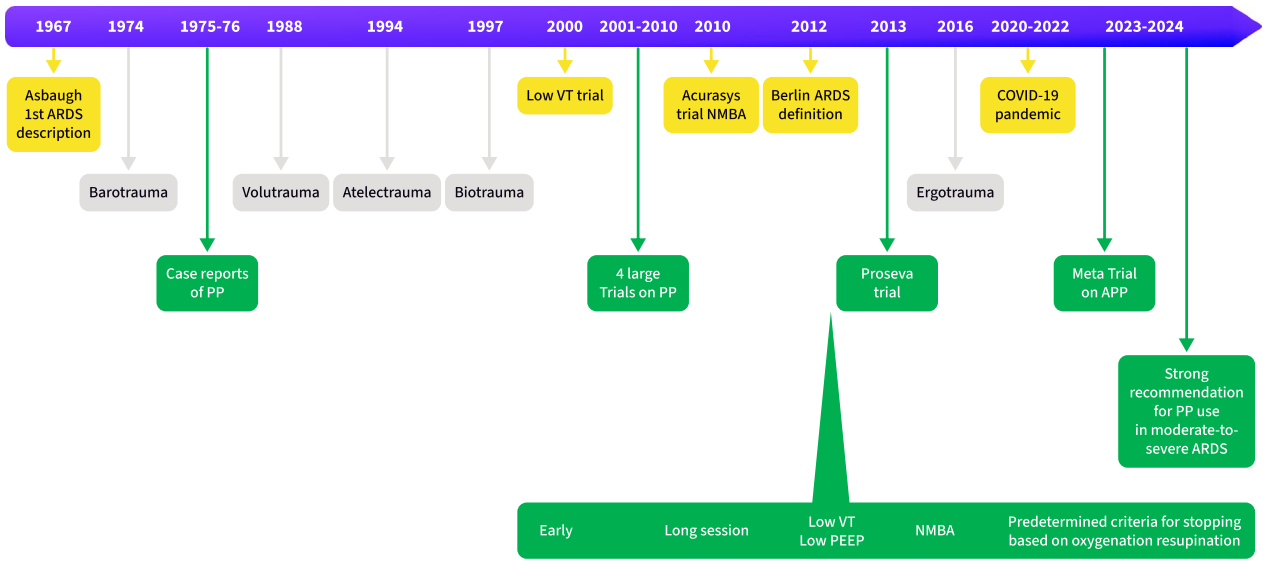

Fig. 2 Trials history of prone positioning. Prone position (green) evidence generation in ARDS patients along a timeline featuring ARDS (yellow) and ventilator-induced lung injury evidence generation (gray). *ARDS* acute respiratory distress syndrome, *VT* tidal volume, *NMBA* neuromuscular blocking agent, *PP* prone positioning, *APP* awake prone position, *PEEP* positive end-expiratory pressure

contingent on treatment adherence. Subsequent evidence suggests that clinical benefits of APP are primarily observed when APP is maintained for prolonged periods (typically beyond 8–10 h per day), with the most recent and comprehensive data also reporting a mortality benefit [39, 41]. Nevertheless, these findings should be interpreted with caution, as the effectiveness of APP in clinical practice is highly dependent on patient compliance.

Guidelines: who, when and how to use prone positioning

In intubated ARDS

Patient selection (Who). The European Society of Intensive Care Medicine (ESICM) expert panel strongly recommends PP in "*intubated patients with moderate-severe ARDS ($PaO_2/F_IO_2 < 150$ mmHg and PEEP ≥ 5 cmH_2O, despite optimization of ventilation settings) to reduce mortality*" [5]. This recommendation is supported by high-quality evidence, primarily driven by the PROSEVA trial. Similarly, the American Thoracic Society (ATS) has updated its previous conditional recommendation in ARDS patients with $PaO_2/F_IO_2 < 100$ mmHg to a strong recommendation in moderate-to-severe ARDS patients [42], reflecting the accumulated evidence base. Whether ARDS sub-phenotypes may help to indicate PP in ARDS patients is unclear and this requires further studies. In the LIVE trial proning patients with a focal ARDS was not associated with lower mortality [43]. We are not aware of data about the effects of PP on patient outcome depending on a hypo- or hyper-inflammatory phenotype. Fosset et al. using machine-learning identified three ARDS sub-phenotypes based on respiratory mechanisms, oxygenation, and demographics in supine position. However, none of them was linked to a change in mortality with PP [44].

The concurrent use of PP and sedation with or without NMBA deserves some discussion about its benefit-to-risk ratio. The data of the ACURASYS [45] and of the PROSEVA trials suggest that both interventions are potentially additive lung-protective adjunctive therapies [46]. The harmful effect of NMBA is not supported by the data: in the ACURASYS trial, the limb muscle strength at 3 months was not different between NMBA and placebo groups. The early use of NMBA associated with light sedation in the ROSE trial found no difference in mortality between NMBA and a control group [47]. The fact that the ESCIM [5] and ATS [42] consensus conferences diverge (a strong recommendation against the routine use of continuous infusions of NMBA in the former and a conditional use of NMBA for the latter) highlights the need for further studies. In line, there is a planned trial (NCT06849570) testing the concurrent role of PP and NMBA after PEEP optimization.

Timing and Initiation (When). The ESICM experts also recommended starting PP "*early after intubation, after a period of stabilization during which low tidal volume is applied and PEEP adjusted and at the end of which the PaO_2/F_IO_2 remains < 150 mmHg*" [5]. A key advance of the PROSEVA trial was the shift from using

PP as a rescue therapy to incorporating it as a core component of lung-protective ventilation, emphasizing early application.

Implementation and Monitoring (How). The ESICM experts stated that "*prone position should be applied for prolonged sessions (16 consecutive hours or more) to reduce mortality*" [5]. However, no formal guideline exists regarding criteria for discontinuation of PP. In practice, trials such as PROSEVA used predetermined oxygenation criteria assessed in the supine position under standardized ventilator settings, rather than relying on transient responses during proning sessions. The use of longer PP sessions, increasingly adopted during the COVID-19 pandemic, remains an area of ongoing investigation. Practical aspects of PP implementation, such as patient positioning (e.g., degree of head elevation) and choice of bed support, are not standardized and generally follow institutional protocols and best practices (Fig. 3). These recommendations are largely based on the PaO_2/F_IO_2 thresholds of the PROSEVA trial, which, beyond the fact that it was a priori working hypothesis to define severe ARDS at that time, is a limitation. Other not filled gaps are the lack of individualization of the duration of the PP session. Tools such as esophageal pressure or electrical impedance tomography may be used to achieve this task.

In non-intubated patients

Patient selection (who). Based on evidence generated during the COVID-19 pandemic, the 2023 ESICM guidelines suggested APP use for non-intubated patients with COVID-19-related acute hypoxemic respiratory failure (AHRF) [5]. However, the strength of this recommendation is tempered by the fact that most high-quality RCT data are derived from COVID-19 cohorts, and the benefit of APP appears conditional rather than universal.

Beyond etiology, patient selection should consider clinical stability, ability to cooperate, and likelihood of response. Meta-analyses suggest that greater benefit may be observed in patients who are younger, receiving advanced respiratory support (HFNC, CPAP, or NIV), with intermediate body mass index, mild-to-moderate hypoxemia, and moderately elevated respiratory rate [41]. Successful implementation requires balancing physiologic suitability with patient tolerance and hemodynamic stability.

Timing and Initiation (When). Although current guidelines do not specify exact timing, available evidence supports early initiation of APP. Post hoc and meta-analyses have demonstrated that initiation within the first 24 h of HFNC or early during hospitalization is associated with improved survival and reduced risk of intubation [41, 48], although the optimal window for initiation remains a subject of ongoing clinical debate.

Implementation and Monitoring (How). While no guideline defines optimal APP duration, it is crucial to distinguish between immediate physiologic efficacy and sustained clinical effectiveness. Although APP frequently yields rapid improvements in oxygenation and respiratory mechanics, translating these physiological gains into tangible clinical benefits remains strictly contingent upon treatment adherence. Accumulating evidence underscores a dose–response relationship between time spent in prone position and clinical benefits, where improved outcomes are associated with prolonged sessions beyond 8 to 10 h per day [41, 49]. Achieving this target often requires a multidisciplinary approach to enhance patient tolerance, including nursing support, patient education, and comfort optimization. Monitoring should include assessment of oxygenation, respiratory rate, and indices, such as the ROX index (SpO_2/F_IO_2/respiratory rate) [50], alongside clinical tolerance and signs of deterioration, to guide continuation or escalation of care.

Physiologic response to prone positioning: prognostic and clinical implications

The response to PP is commonly assessed using intermediate physiologic variables, most frequently changes in PaO_2 or PaO_2/F_IO_2, measured either during PP or after resupination. Other parameters, such as $PaCO_2$, respiratory mechanics, or EIT-derived indices, are less frequently used in routine practice.

Several studies have investigated whether physiologic responses to PP can predict clinical outcomes (Table S2). Multiple observational studies have reported that early improvement in oxygenation during or shortly after the initial PP session is associated with favorable outcomes, including reduced ICU mortality, improved survival without extracorporeal membrane oxygenation (ECMO), and increased ventilator-free days (Table S2). In contrast, secondary analyses of the PROSEVA trial did not demonstrate a survival difference between oxygenation responders and non-responders after the first PP session (Table S2). This inconsistency raises an important conceptual question: whether physiologic response to PP primarily reflects lung recruitability or is influenced by baseline disease severity [51]. Improvement in oxygenation may identify patients with greater potential for recruitment and improved ventilation–perfusion matching. However, oxygenation response may also be influenced by factors unrelated to lung protection, including pulmonary perfusion, chest wall mechanics, and ARDS morphology. Conversely, patients without substantial oxygenation improvement may still derive benefit from PP through reduction and homogenization of regional lung stress and strain. These observations suggest that oxygenation response alone may not fully capture the

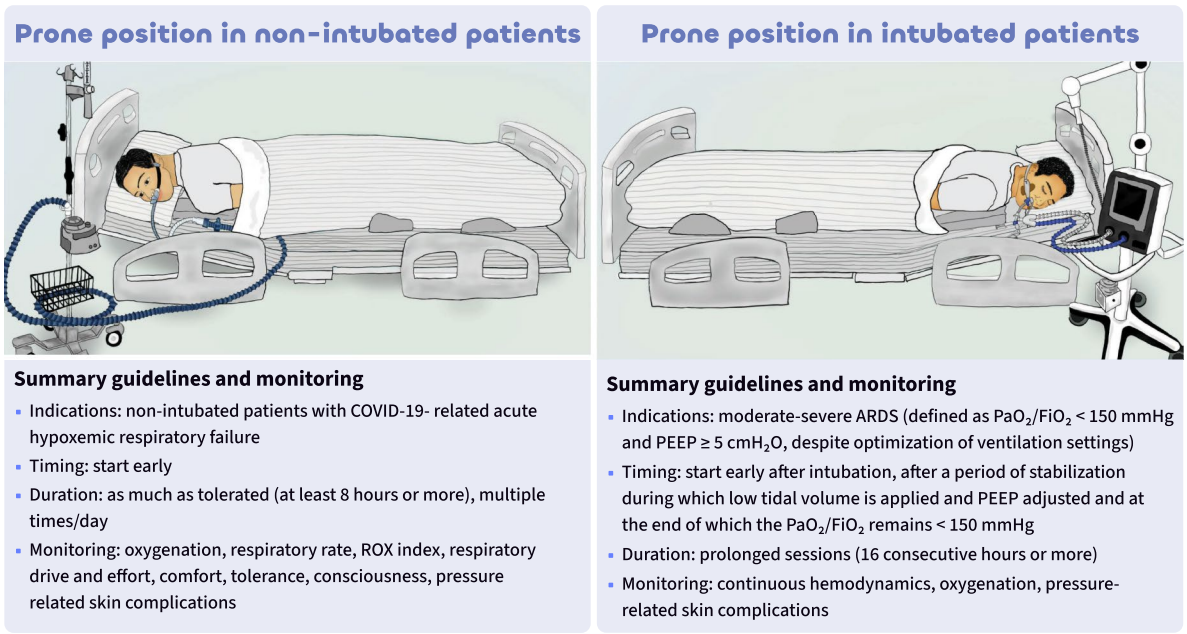

Fig. 3 Summary guidelines and prone positioning monitoring in non-intubated and intubated patients. *COVID-19* coronavirus disease 2019, *ROX* respiratory rate-oxygenation index, *ARDS* acute respiratory distress syndrome, *PEEP* positive end-expiratory pressure, PaO_2 arterial partial pressure of oxygen, F_IO_2 fraction of inspired oxygen

complex physiologic and protective effects of PP. In contrast to transient improvement during a single session, persistent oxygenation improvement after resupination or during subsequent PP sessions appears to have greater prognostic value and may better reflect lung recruitability, although supporting evidence remains limited (Table S2). Beyond oxygenation, several studies have explored additional physiologic prognostic markers, and found reduction in $PaCO_2$ during PP (reflecting improved alveolar ventilation and reduced dead space), better respiratory system compliance during PP or after resupination, and enhanced ventilation–perfusion matching within 4 h of the first PP session (Table S2).

In nonintubated patients, similar approaches have been explored. Improvements in oxygenation during APP have been associated with a lower likelihood of intubation in some analyses, although findings are inconsistent (Table S2). Imaging-based responses may provide additional prognostic information; for example, increased dorsal lung aeration assessed by lung ultrasound after the first APP session has been associated with a reduced risk of intubation [52].

Overall, these findings suggest that physiologic responses to PP, particularly sustained improvements in oxygenation, CO_2 clearance, lung mechanics, or regional aeration, may help identify patients who are more likely to benefit from this intervention. However, the available evidence remains largely observational, and no validated physiologic criteria exist to guide decisions regarding continuation or termination of PP. Consequently, there is insufficient evidence to support using physiologic response alone to determine whether PP should be maintained or stopped in clinical practice.

Adverse events, workload, and contraindications

Prone positioning, whether applied in intubated or non-intubated patients, is generally safe when implemented by trained teams, but it is associated with distinct profiles of side effects and contraindications. Although PP does not incur direct material costs, it carries significant workload implications [6]. In intubated patients, complications are relatively common but typically manageable. Pressure injuries represent the most frequent and dose-dependent adverse event, particularly with prolonged sessions [53–58]. Other complications include facial edema, transient hemodynamic instability during position changes, and less frequent but potentially serious events, such as unplanned extubation, device dislodgement, peripheral nerve injury, and ocular complications [53, 54, 59]. Importantly, unstable spinal injury remains the single widely accepted absolute contraindication, while other historical and theoretical relative contraindications, such as obesity, recent surgery, the presence of drains should not refrain experienced teams of proning patients [6, 53, 60]. PP in intubated patients is resource-intensive, typically requiring 3–5 trained staff per

maneuver, with workload concentrated during position changes [2, 6, 61]. In contrast, APP is associated with a markedly lower incidence of adverse events, with intolerance, discomfort, and pain being the primary limiting factors, and only occasional minor complications, such as superficial skin injury or device displacement [34, 41, 62, 63]. APP imposes a different type of workload, requiring sustained monitoring, patient coaching, and frequent reassessment to ensure adherence throughout the session [61].

Implementation in daily clinical practice

Despite strong evidence supporting its use, the implementation of PP has historically been inconsistent, with substantial temporal and regional variability. Before the COVID-19 pandemic, large international studies demonstrated marked underutilization. In the LUNG SAFE study, PP was applied in fewer than 20% of patients with severe ARDS [64]. Similarly, the APRONET study showed that even among patients meeting established criteria ($PaO_2/F_IO_2 < 150$ mmHg), only a minority were proned, highlighting poor adherence to guideline recommendations [65]. Although uptake was slightly higher in Western Europe, where most landmark trials (including PROSEVA) were conducted, overall utilization remained low, particularly in North America, where PP was often reserved as a rescue therapy [66–68]. The fact that the PROSEVA trial included selected ARDS patients may legitimate clinicians to not apply it. This reluctance was, however, not observed among COVID 19 patients despite an evidence background similar to before the pandemic. Indeed, the pandemic led to a rapid and substantial increase in PP use, although regional differences persisted. In several European cohorts, PP was applied in the majority of intubated patients, with reported rates of 60–80% among eligible individuals [69–71]. In contrast, North American studies reported more modest use, with only one-third to one-half of eligible patients receiving early PP, and up to 47% never undergoing PP [72–74]. Even greater variability has been reported outside Western countries [75].

For non-intubated patients, APP was widely adopted during the COVID-19 pandemic, often ahead of high-quality evidence. Nevertheless, implementation remains inconsistent. For example, in a cohort of 16 Dutch ICUs, only 16% of eligible non-intubated patients received APP [76]. Potentially higher utilization has been reported in selected cohorts [30].

In the post-pandemic period, improvements in PP implementation appear only partially sustained. In North America, early PP is now applied in approximately 30–40% of eligible patients, substantially higher than pre-pandemic levels but still below pandemic peak [77].

Overall, these data highlight a persistent gap between evidence and practice. Despite some clear clinical evidence for its efficiency, PP remains underutilized, with implementation largely influenced by system-level factors such as staffing, training, and protocolization rather than evidence alone. Multilevel exploration of barriers to implementation, at the individual level like clinicians' belief, circadian staffing variability, and unit case mix but also at the systemic level, such as national staffing heterogeneity, ICU cost and funding models is warranted. Indeed, while scientific evidence might be high, resources available for proning and other interventions being constrained, prioritization may occur. Conversely additional resources may be ineffective on other barriers, such as clinicians' belief, for example.

Questions currently under investigation

Awake prone position in non-COVID acute hypoxemic respiratory failure. APP has been widely adopted to treat COVID-19-related acute hypoxemic respiratory failure, whereas its role in non-COVID etiologies remains poorly defined. Prior to the pandemic, five small case series and observational studies suggested that APP could improve oxygenation [78]. More recently, a prospective physiologic study including 10 patients with non-COVID acute hypoxemic respiratory failure treated with HFNC reported that 30 min of APP significantly improved lung ventilation homogeneity, with effects persisting after resupination [79]. However, RCTs evaluating clinical outcomes such as intubation and mortality in non-COVID patients are lacking. Three large RCTs are currently ongoing. The PRONELIFE trial aims to enroll 650 patients from 35 ICUs worldwide and evaluates endotracheal intubation within 14 days [80]. Another multicenter trial conducted in 42 hospitals in the United Kingdom plans to enroll 1,708 patients and assesses intubation within 30 days after randomization (ISRCTN63784375) and a trial in France will randomize 1,078 patients with non-COVID community acquired pneumonia receiving HFNC to assess intubation at 28 days (NCT06966310). Given the heterogeneity of acute hypoxemic respiratory failure etiologies and respiratory support strategies, the magnitude of benefit from APP may vary substantially across these patient populations.

Proning in mild-to-moderate intubated ARDS. The PROMILD trial (NCT05056090) is an ongoing RCT evaluating early PP in mechanically ventilated patients with mild-to-moderate ARDS. The primary outcome is ventilator-free days, with additional endpoints, including mortality and duration of mechanical ventilation. This trial will help clarify whether PP should be extended to patients with less severe ARDS.

Long sessions of proning in intubated ARDS patients. Prolonged PP, typically defined as sessions exceeding the conventional 16-h duration, has recently been explored as an alternative strategy in ARDS. Beyond effects on clinical outcomes, reduced resource burden might be expected due to less frequent turning procedures.

However, a recent systematic review and meta-analysis including nine studies (n = 1,045) found no significant effect of prolonged PP on 90-day mortality or other clinical outcomes, with low to very low certainty of evidence [81]. Importantly, most included studies, including all three RCTs, enrolled patients with COVID-19 ARDS, limiting generalizability. A subsequent RCT comparing 16-h vs 24-h prone sessions likewise found no differences in clinical outcomes, although > 85% of patients had non-COVID ARDS [82], expanding the evidence beyond COVID-19 populations. Ongoing trials, including NCT06854627, are evaluating even longer continuous proning strategies (48–120 h).

Prone positioning in ARDS receiving VV-ECMO. Two RCTs have evaluated PP vs supine positioning during veno-venous ECMO in severe ARDS, with inconsistent results likely explained by differences in patient characteristics and baseline severity. In the PRONECMO trial, > 95% of patients had already undergone PP prior to ECMO initiation, suggesting a more severe and refractory population [83], whereas in Tong et al.'s study < 15% of patients received PP before ECMO [84]. This difference likely contributed to the higher rates of successful ECMO weaning within 30 days and the shorter ECMO duration observed in Tong et al.'s cohort. In addition, the PRONECMO trial included predominantly COVID-19 patients (> 90%), while approximately half of patients in Tong et al.'s study had COVID-19. Consistent with these findings, a recent meta-analysis suggests that the potential benefits of PP during ECMO may be greater in non-COVID ARDS populations [85].

Should another trial on PP in moderate-to-severe ARDS patients be done? The question arose during the ESICM consensus conference and was judged unlikely given the lack of equipoise in the field. However, as mentioned above, there is an ongoing trial testing different durations of proning sessions in moderate-to-severe ARDS. In addition, the assessment of lung ventilation distribution at the bedside, well-designed hypothesis-driven trials may be used to better define the duration and repetition of proning session, just as an example of a potential trial. Overall, future studies should move beyond simply determining whether PP is beneficial and instead focus on identifying which patients are most likely to benefit, when PP should be initiated, and how its delivery can be optimized across different clinical settings. Better integration of physiologic monitoring, refinement of implementation strategies, and improvement in patient tolerance and adherence may help maximize the effectiveness of PP in both intubated and nonintubated patients.

Prone positioning strategies for future pandemics

In the event of a future COVID-like pandemic, proning should evolve from a reactive rescue therapy into a proactive standard of care. One of the key lessons from the COVID-19 pandemic is that PP represents a high-value, low-cost intervention capable of alleviating ICU "surge capacity".

Future strategies should prioritize early initiation and individualized, response-guided application. For nonintubated patients, APP should be integrated into standardized clinical care pathways to prevent intubation. Rather than a universal mandate, clinical decision-making should focus on identifying potential responders using bedside physiologic markers.

Successful large-scale implementation of proning, will depend on optimizing both team performance and patient adherence. Protocols should emphasize "comfort-driven proning" strategy, including ergonomic positioning, and the use of pressure-redistribution devices to prevent complications, such as pressure injuries or nerve compression. Moreover, the "dose–response" relationship underscores the importance of achieving adequate daily duration (e.g., 12–16 h), which may be facilitated by dedicated multidisciplinary "Prone Teams". These teams can ensure safe positioning, enhance patient tolerance, and maintain adherence over prolonged sessions. Finally, preparedness for future pandemics should include the development of standard operating procedures, structured training programs, and scalable implementation models during inter-pandemic periods. At the same time, targeted research efforts are needed to address remaining knowledge gaps and generate high-quality evidence to further refine the role of PP across different patient populations and clinical settings.

Conclusions

Prone positioning confers important physiological and patient-centered benefits in both intubated and non-intubated patients with ARDS. Supported by high-quality RCTs demonstrating a survival benefit, PP has evolved from a rescue therapy for refractory hypoxemia into a cornerstone of evidence-based management. The COVID-19 pandemic further accelerated its adoption, particularly in non-intubated patients. However, growing evidence suggests that the clinical benefits of APP remain conditional, reflecting a dose–response relationship driven by treatment adherence. Nowadays, PP occupies a central role in ARDS management and is recommended by international guidelines across a broad spectrum of disease severity and respiratory support strategies.

Despite these advances, key uncertainties persist. The effectiveness of PP in non-COVID-19 ARDS among

non-intubated patients, its role during ECMO, the optimal duration of prolonged sessions, and its benefit in mild-to-moderate ARDS remain incompletely defined. Looking forward, lessons from the COVID-19 pandemic underscore the importance of early implementation, system-level preparedness, and rapid evidence generation. Continued high-quality research is essential to refine patient selection, optimize protocols, and ensure the safe and effective application of proning across diverse clinical contexts.

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Declarations

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Ethical approval
This article does not contain any studies with human participants or animals performed by any of the authors.

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